

What Is Claimed Is:

1. A modified nucleotide compound which includes at least one component selected from the group consisting of MN_3M , $B(N)_xM$ and $M(N)_xB$ wherein:

N is a phosphodiester-linked modified, ^{or unmodified} or unmodified 2'-deoxynucleoside moiety;

M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;

B is a moiety that confers exonuclease resistance to the terminus to which it is attached;

x is an integer of at least 2.

2. The modified nucleotide compound of claim 1 wherein M and B are the same moiety.

3. The modified nucleotide compound of claim 1 which, when in complex with a complementary RNA, confers RNase H sensitivity to the RNA.

4. The modified nucleotide compound of claim 1 wherein N contains at least one adenine, guanine, thymine or cytosine moiety.

5. The modified nucleotide compound of claim 1 wherein N contains at least one uracil, inosine or 2, 6-diaminopurine moiety.

6. The modified nucleotide compound of claim 1 wherein N contains at least one 5-halogenated uracil or cytosine or a substituted or unsubstituted 7-deazaguanine, 7-deazaadenine or 7-deazainosine moiety.

7. The modified nucleotide compound of claim 1 wherein N contains at least one methylated adenine, guanine, thymine or cytosine moiety.

8. The modified nucleotide compound of claim 1 wherein M is a C_1 - C_4 alkylphosphonate deoxynucleotide.

9. The modified nucleotide compound of claim 8 wherein M is a methylphosphonate deoxynucleotide.

10. The modified nucleotide compound of claim 1 wherein M is an alpha-phosphodiester 2'-deoxynucleoside.

11. The modified nucleotide compound of claim 1 wherein M is selected from the group consisting of an aminophosphonate, phosphotriester, phosphoramidate, carbamate or morpholino-substituted nucleotide.

12. The modified nucleotide compound of claim 1 wherein B is directly or indirectly attached to the deoxyribose moiety of at least one of the 3'- and 5'-terminal nucleotides.

13. The modified nucleotide compound of claim 12 wherein B is directly or indirectly attached to a hydroxyl group of the deoxyribose of at least one of the 3'- and 5'- terminal nucleotides.

14. The modified nucleotide compound of claim 12 wherein B is directly or indirectly attached to a phosphate moiety attached to the deoxyribose moiety of at least one of the 3'- and 5'- terminal nucleotides.

15. The modified nucleotide compound of claims 13 or 14 wherein B is selected from the group consisting of an intercalating agent, an isourea, a carbodiimide and an N-hydroxybenzotriazole.

16. The modified nucleotide compound of claim 13 wherein B is a methylthiophosphonate.

17. The modified nucleotide compound of claims 13 or 14 wherein B is a polypeptide or protein.

Red 121
~~18. The modified nucleotide compound of claim 1 which includes at least one sequence of the formula $M(N)_x B$ wherein B is a modified or unmodified 2', 3'-dideoxyribose nucleotide.~~

~~19. The modified nucleotide compound of claim 1 wherein x is an integer selected from the group consisting of 2 or 3.~~

~~20. A modified nucleotide compound which contains at least one sequence having the formula MN_3M wherein N is a phosphodiester-linked unmodified~~

2'- deoxynucleoside moiety containing at least one guanine, adenine, cytosine or thymine moiety and M is a methylphosphonate-containing deoxynucleotide.

- Sub
3 E2
21. A method of inhibiting the function of an RNA, which comprises: contacting said RNA, under conditions permissive of hybridization, with a modified nucleotide compound which includes at least one complementary component selected from the group consisting of MN_3M , $B(N)_xM$ and $M(N)_xB$ wherein:

N is a phosphodiester-linked modified ^{or unmodified} 2'-deoxynucleoside moiety;

M is a moiety whose presence confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base;

B is a moiety whose presence confers exonuclease resistance to the terminus to which it is attached; and

x is an integer of at least 2.

22. The method of claim 21 wherein the RNA is contacted with a compound wherein M and B are the same moiety.

23. The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one adenine, guanine, thymine or cytosine moiety.

24. The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one uracil, inosine or 2, 6-diaminopurine moiety.

25. The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one 5-halogenated uracil or cytosine or a substituted or unsubstituted 7-deazaguanine, 7-deazaadenine or 7-deazainosine moiety.

26. The method of claim 21 wherein the RNA is contacted with a compound wherein N contains at least one methylated adenine, guanine, thymine or cytosine moiety.

27. The method of claim 21 wherein the RNA is contacted with a compound wherein M is a C₁-C₄ alkylphosphonate.

28. The method of claim 27 wherein the RNA is contacted with a compound wherein M is a methylphosphonate.

29. The method of claim 21 wherein the RNA is contacted with a compound wherein M is an alpha-phosphodiester 2'-deoxynucleoside.

30. The method of claim 21 wherein the RNA is contacted with a compound wherein M is selected from the group consisting of an aminophosphonate, phosphotriester, phosphoramidate, carbamate or morpholino-substituted nucleotide.

31. The method of claim 21 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to the deoxyribose moiety of at least one of the 3'- and 5'- terminal nucleotides.

32. The method of claim 31 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to a hydroxyl group of the deoxyribose of at least one of the 3'- and 5'- terminal nucleotides.

33. The method of claim 31 wherein the RNA is contacted with a compound wherein B is directly or indirectly attached to a phosphate group attached to the deoxyribose moiety of at least one of the 3'- and 5'- terminal nucleotides.

34. The method of claims 32 or 33 wherein the RNA is contacted with a compound wherein B is selected from the group consisting of an intercalating agent, an isourea, a carbodiimide and an N-hydroxybenzotriazole.

35. The method of claim 32 wherein the RNA is contacted with a compound wherein B is a methylthiophosphonate.

36. The method of claims 32 or 33 wherein the RNA is contacted with a compound wherein B is a polypeptide or protein.

37. The method of claim 21 wherein the RNA is contacted with a compound which includes at least one sequence having the formula $M(N)_x B$ wherein B is a modified or unmodified 2', 3'- dideoxyribose nucleotide.

38. The method of claim 21 wherein the RNA is contacted with a compound wherein x is selected from the group consisting of 2 or 3.

39. The method of claim 21 wherein the RNA is contacted with a modified nucleotide compound which includes at least one sequence having the formula MN_3M wherein N is a phosphodiester-linked unmodified 2'-deoxynucleoside moiety containing at least one guanine, adenine, cytosine or thymine moiety and M is a methylphosphonate-containing deoxynucleoside.

40. A method of identifying a nucleotide compound having a combination of nuclease resistance and the ability to form an RNase H substrate when in complex with an RNA, which method comprises:

- (i) preparing modified nucleotide compounds;
- (ii) selecting by exo- and endonuclease digestion those modified nucleotide compounds of (i) which are nuclease-resistant as shown by being capable of forming and electrophoretically migrating as a duplex with a complementary nucleotide compound; and
- (iii) selecting by RNase H digestion those of the nuclease-resistant nucleotide compounds of (ii) which act as substrates for RNase H when hybridized with a complementary RNA.

41. A method of treating a human or animal so as to inhibit the function of a target RNA therein which method comprises administering a therapeutically effective amount of a modified nucleotide compound so as to inhibit the function of the target RNA, which modified nucleotide compound includes at least one component selected from the group consisting of MN_3M , $B(N)_x M$ and $M(N)_x B$; wherein N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety, M is a moiety that confers endonuclease resistance on said component and that contains at least one modified or unmodified nucleic acid base, B is a moiety that confers exonuclease resistance to the terminus to which it is attached and x is an integer of at least 2.

Sub E3 / 42. A compound containing at least 1 exonuclease and endonuclease resistant component consisting of 2 or more contiguous phosphodiester-linked 2'-deoxynucleosides.

43. The compound of claim 42 which is capable of specifically binding with a nucleic acid sequence of interest to inhibit the function thereof.

44. The compound of claim 42 which, when complexed with a complementary RNA, confers RNase H sensitivity upon the RNA.

45. The compound of claim 42 which comprises an oligonucleotide or polynucleotide.

46. The compound of claim 45 wherein the oligonucleotide or polynucleotide is modified.

47. The compound of claim 46 wherein the modified oligonucleotide or polynucleotide consists of at least one moiety which confers endonuclease resistance and at least one moiety which confers exonuclease resistance.

48. The compound of claim 47 wherein the endonuclease-resistance conferring moiety also confers exonuclease resistance to the modified nucleotide component.

49. The compound of claim 47 wherein the portion of the compound that can function as an RNase H substrate is located between the moiety conferring exonuclease resistance and the moiety conferring endonuclease resistance.

Sub E4 / 50. A compound containing an endo- and exonuclease resistant sequence which consists of 2 or 3 contiguous phosphodiester-linked 2'-deoxynucleosides.

add a'
add a'
Enz-47